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Nuclein in Paralysis Agitans

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The Diagnosis and Treatment of Dementia Praecox

The Application of Nuclein to Its Arrest

By BAYARD HOLMES, B. S., M. D., Chicago, Illinois

DEMENTIA præcox, or the insanity of adolescence, occupies a unique place in medical practice and medical literature. It is not mentioned in Osler's "Modern Medicine," nor in his textbook, of which 100,000 copies have been sold! Fifteen thousand youths afflicted with this "disease," however, are committed to the madhouses of the United States each year, and they are pronounced incurable from the start. The management of these madhouses in Illinois (for example) is in the hands of five politicians, only one of whom is required by law to have any medical training or any knowledge of the problems of insanity.

No layman, and but few physicians, will believe me or anyone else when, in utmost seriousness and humiliation, we assert that *no effort is made* by any member of the Board of Administration in Illinois or by any of the faculties of the ten institutions under their direction to study the conditions of these unfortunate youths. The eight superintendents, who are political appointees, are full of "business," feeding, housing, and attending the many social needs of their irresponsible and helpless wards. The medical care of these unfortunates is intrusted to young physicians who have had little or no experience, and who get out of the service as soon as they can, if they are good for anything, because they cannot endure the unprofessional conditions of their environment.

When a youth suffering from dementia præcox is committed to one of these institutions he is locked into the ward, where he becomes noisy and boisterous or sullen and silent. In the former case, he is likely to be "beaten up" by the "nurse attendants" until thoroughly cowed and humbled. The attendants are omnipotent and remain in the institutions through all changes of adminis-

tration. If catatonic, the patient curls up in bed and starves. The death rate during the first year is high. At the end of this year there is apt to occur a change—an adaptation. The emaciated patient—with swollen tongue, jaws protruding like an ape's, teeth rotting from neglect, hands, feet, legs, arms deformed from catatonia, abdomen and cheeks retracted from starvation—begins to wake up and become active or, on the other hand, he sinks to lower depths. During the first year of confinement to bed the patient is filthy half the time, lying in a bed wet in his own urine and befouled with his own offal—a picture of neglected misery that cannot be described, and that cries to civilization for correction or else euthanasia.

With this terrible picture, putting 300 great blots on the map of the United States where over 120,000 dementia-præcox patients are consigned to a pessimistic and nihilistic custody; with the boards of control of forty-eight sovereign states, expending for this custody of these wrecked citizens nearly \$50,000,000 annually, or four-tenths of the budget of the several states; with a suffering, but ignorant public, composed of the friends of the insane behind them and begging for betterment; with all these things, I say, they make no effort, spend no money and encourage no sacrifice for research for discovering the cause of this grave malady, or for finding some cure or way of prevention.

In Illinois, a research-institute was established by the Code of Charities (1907) but, with a legislative appropriation of over \$17,300, only two men are employed in its Psychopathic Institute.

How to Study Dementia Præcox

Fortunately, during the past year and a half, the application of the Abderhalden reac-

tion to psychiatry has proved, beyond a possibility of discussion, that dementia præcox is a "disease," of which the mental symptoms and the deterioration are but incidents. Dementia præcox is not a perversity of conduct, a twisted idea or a curse of God. It is shown by this reaction that the pancreas and the genital glands are undergoing a degenerating process, as liver does in alcoholism and the thyroid gland does in exophthalmic goiter.

This terrible disease is slow in its onset, as a rule, and is characterized by a peculiar pupillary condition, a peculiar loss of weight, a peculiar perspiration, a peculiar arrest of growth of hair, a peculiar atrophy of the lower leg, and a peculiar condition of the blood. One may learn to recognize the disease by the two clinical methods: that of the asylum, where many cases can be studied in many stages of the disease, most of them in terminal conditions; and that of the physician, who sees one or two cases often in each succeeding stage of the disease. There is no doubt that each of these clinical methods has relatively some advantages over the other.

There are two more methods of studying the disease that ought to be utilized, but which are rarely employed. They each offer to the serious student employing either of the previous methods (the superficial study of many in a short time or the intensive study of a few over a long time) the greatest assistance in correcting misconceptions.

The laboratory method has been little used, and can be fully utilized only in the large general hospital, with a research-institute attached, like that at the Michael Reese with its Morris Institute or that at the Presbyterian with the Institute for Infectious Diseases, both of Chicago. There has been little laboratory study of dementia præcox. Even the condition of the blood has been only superficially observed, and hardly any coordinate studies of blood, metabolism, and conduct have been made. Therapeutic and laboratory investigation have not been undertaken.

The study of the literature of any medical subject is necessary to a full comprehension of all its intricacies. The literature of dementia præcox, under that name, is only twenty-five years old, but, now having the clinical entity well in mind, we can go back through the European literature of three hundred years and recognize the type; also even in the ancient Egyptian (in the Papyrus Ebers) for example, 1500 B. C., a clear

picture of the disease is discovered. All four of the methods of studying the disease are necessary for its comprehension; namely: the prolonged and intensive study of one case, the superficial study of many cases, the laboratory study of one or many cases, and the reading of the world literature of the whole subject.

Dementia Præcox Characterized

From such a study as this, we conclude that dementia præcox is a condition appearing usually at the beginning of adolescence. It may make itself known at any later period. Its earliest manifestations are metabolic, and associated with various symptoms. In one case, it is simply nutritional; in another, skeletal; in still another, glandular. Various accidents and sicknesses precipitate the disease. The joints, the apophyses, the teeth, the tonsils, the intestinal functions are all and each apt to feel the intoxication. The use of the Abderhalden reaction in early cases has not as yet been reported, but one can readily guess that some remarkable disclosures in this direction are bound soon to appear.

The mind of the patient is apt to be greatly stimulated and the patient is prone to overdo in the beginning, but his vision and genius-like labor is followed by inactivity, depression, and apparent dementia. There are illusions, hallucinations, and delusions of mind, which results in errors of conduct; but dementia does not actually come on, and the patient, starving, mute, dirty, inactive, and fed with a tube, is perfectly conscious of his surroundings and remembers everything, has regrets and remorse, terror and fear, and suffers all the pain that rational persons do. These subjects are also perfectly cognizant of ill treatment and kind treatment, but their delusions modify their conduct. They perceive, they conceive, but they cannot execute. In catatonia, they have muscular rigidity and in its early stage the condition is denominated negativism.

From a similar quadrajugate study, we conclude that there is no etiology, pathology or treatment of this disease yet recognized. The prognosis is always bad. Recovery is unknown. The duration of the disease is unlimited. While many cases terminate early in death, the great majority live to acquire tuberculosis or other intercurrent or institutional diseases, and die—five, ten, twenty or more years after commitment. The disease rests at times and the patient becomes an uncomplaining drudge about the

asylum, after earning a man's wages for the state.

Enter The Abderhalden Reaction

The first light is thrown upon this disease by the Abderhalden defensive-ferment reaction. This method, introduced by Fauser¹, of Stuttgart, in February, 1913, and continued by him and by a great army of biologic chemists and serologists in Europe, has shown that the genital glands are disturbed in every case of dementia præcox—the ovaries in females, the testicles in males. In catatonic cases, the thyroid gland also is disturbed. In every advanced, severe and terminal condition, brain-cortex also is involved. The later, and perhaps more happy, work of Fuchs and Fremd², shows that the pancreas is as early disturbed as the genital glands, perhaps even earlier. The patients afflicted with other insanities, especially manic depressive insanity, show none of these reactions.

Our study of the literature of this terrible disease, the etiology and pathology of which are unknown, shows little hope of successful treatment. Some do get well, especially after an attack of the infectious diseases, and now and then a recovery is reported; just as in the seventeenth, the eighteenth and the early part of the nineteenth centuries cases of successful laparotomies were reported. In Massachusetts, when one out of 1500 admitted were reported recovered during a seven-year period under examination, the medical officer making the report was severely criticized.

Now it has happened that Bruce, Dide, Fischer, Halvar Lundvall, and Julius Donath have reported recoveries by the production of an artificial hyperleukocytosis, and this is the reason for writing this paper.

Has a Cure Been Discovered?

Lundvall made the most careful and extensive examination of the blood of the insane under his care, and developed the observation that there exists a polycythemia and leukopenia when the dementia præcox patient is failing, and a hyperleukocytosis and normal number of red corpuscles when the patient is improving.

In England and on the Continent, the nucleinate of sodium has been used to increase the leukocytes and produce improvement. One of the great objections to the use of this

agent was the large quantity of water—50 to 100 Cc.—necessary, and the pain resulting from the injection of the large doses employed. Ittau, Fischer, and Donath have reported betterment, and even recoveries from its use. Julius Donath, in a recent essay, charges the psychiatrists with unwarranted pessimism toward dementia præcox, and reports actual recoveries after the use of sodium nucleinate.

Lundvall's Prescription

The most important and significant contribution to the treatment of dementia præcox comes from Halvar Lundvall, of Lund, Sweden. He uses a very concentrated solution, and has reported 18 cases, of whom 6 actually recovered, and all but 3 made remarkable and very desirable improvement. His report was obscurely published more than a year ago, and some improvements have been made in the preparation of the remedy at the "Apotheke Kjorten" in Lund. The remedy is prepared according to the following formula:

Quassini depurati sicci. Gm. 2.0
Aquæ destillatæ. Cc. 50.0
Boil in a water-bath for one and a half hours,
filter, and add
Hetoli (i. e. sodii cinnamati) . . Gm. 1.0
Sodii nucleinati. Gm. 10.0
Acidi arsenosi (in solution) . . Gm. 0.005
Boil until all is dissolved, filter, and add
Aquæ destillatæ bullientis, q. s.
ut fiat. Cc. 50.0

This remedy should be kept in a dark, cool place. It does not need to be resterilized.

In anticipation of the use of this remedy, the patient's blood should be examined and the leukopenia demonstrated and recorded; the bowels should be opened with calomel at night and a saline laxative in the morning, followed by an enema consisting of 4 quarts of hot water (105° F.), to which a tablespoon full of glucose (corn-syrup) has been added.

Then 1 or 2 cubic centimeters of the remedy is injected into the buttocks or other neutral place. In about six hours and after a slight chill, the temperature will be found to be 102° or 103° F., and the leukocytes will rise to 20,000 or even higher. The red corpuscles will go down nearly to normal, falling from 6,000,000 or higher to 5,000,000 or even to 4,500,000. There is usually an increase in urine. The reaction is stronger after the first and earlier injections, and later it is necessary to increase the dose even to 15 or 20 Cc.

The only guide as to the time for the next injection is the examination of the blood.

¹Fauser, A. D. m. W., Feb. 13, 1913, Vol. 39, p. 304-307.

²Fuchs & Fremd. M. m. W., Feb. 10, 1914. Vol. 61 pp. 307-310.

The temperature stays up only a few days, but the leukocytes, in one of my cases, remained above 25,000 for five weeks. When the leukocytes fall below 12,000, then the dose should be repeated. When the reaction, as measured by the leukocytes, begins to weaken, the dose should be increased by 1 or 2 cubic centimeters.

Treat Like Tuberculosis

During all the time, the patient should be treated like a tuberculosis patient. Cold air, sunshine, and a good feeding—3000 to 5000 calories a day—are desirable. The daily bath and glucose enemas keep the patient clean and tidy. If the patient is mute and inactive, he must be taken to the toilet regularly, and great care must be taken with his teeth. Calomel and laxative salines often are necessary.

When it is possible, the patient should be exposed to the sunlight, cold air, and rain, just as Dr. A. Rollier, of Leysin, treats his patients suffering from surgical tuberculosis. ("Ergebnisse der Chirurgie und Orthopödie," Vol. 7, p. 1 to 146), and *Interstate Medical Journal*, March, 1914, Vol. 21, p. 279 to 284.

The uniform effect of these injections has been noticed by every one. There is a change. Every patient whom I have injected has gained weight, one as much as 20 pounds in six weeks. This is what might be expected, as the Abderhalden reaction shows a *dysfunktion* of the pancreas—and the pancreas is the lipase generator, the enzyme of fat metabolism.

It will be noticed that the hair grows more rapidly. If the forty-eight hour growth of the beard on a definite part of the face, cut before injections are used, is carefully laid on gummed paper or, better, measured with a micrometer, it will be found that, after the injections, the forty-eight-hour growth is at least half as long again. One mute catatonic, weighing less than 80 pounds, who had been fed with a nasal tube for three months, was led to the table a few days after the second injection and, with a little urging, fed himself. Interest in life increased in one young man, and he said he was "urged from

within himself to eat and exercise and try to get well."

None of my patients treated with Lundvall's remedy have been examined by the Abderhalden method, but there was no doubt in any case of the diagnosis of dementia præcox. Every state institution ought to be able to make Abderhalden tests, and then this hopeful and promising remedy could be given an adequate and a conclusive trial.

Don't expect too much in a short time. Keep up the remedy with every possible improvement in the general hygienic conditions. As soon as interest can be aroused, cultivate it, but do not exhaust the patient. One young man, who had not written or spoken a word for four years, on several occasions, wrote his own name, after a little urging, after the sixth injection, and after a gain in tidiness and disposition that rendered his attendants grateful. His weight increased 10 pounds during the same time, he stood up straighter and walked better, going two or more miles twice a day.

Although I have used the remedy on only a few patients for six months, and every patient has improved, some have become more troublesome for the time. In an institution, the troublesome patient gets himself disliked.

It seems to me the remedy should be thoroughly tried, as it is painless and produces no abscesses. It is a thoroughly rational procedure. The patient's weight increases under its use. The inactive patients become active and thus cause more trouble, but they could hope to recover only by becoming more active.

The publicity given the method by *The Literary Digest* of March 7, has brought me a large correspondence and has aroused several centers of active therapeutics for this condition. I have in every case answered the letters and begged for reports of success or failure, and I shall hope to have a more exact and comprehensive report in a few months.

The editors of this journal have undertaken to assist in furthering the treatment by supplying the remedy for experimental use when it can be administered under reasonable and favorable conditions.



Experiences With Nuclein in the Treatment of Insanity^{*}

By FRANZ HAUBER, M. D., Rufach, Germany

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INSPIRED by the success of Fischer, Donath, Van Wagner, and Pilcz in the treatment of progressive general paralysis with tuberculin and nuclein, the author started his work along these lines in 1910, and has continued systematically since then. The preparation employed by him is sodium nucleinate; this substance being preferred to tuberculin—which not always is harmless—while having the same general effect as the latter. All paretics were subjected to the treatment, as were also all the completely demented paretics—for the sake of control—although no results were anticipated in their case.

After the first favorable results, especially those obtained in recent cases of general paralysis, the author extended his experiments also to cases of dementia præcox. All those relatively recently diseased, especially the excited catatonics, received the injections systematically; for experience had shown that in them periods of improvement would occur sooner than in the inveterate. A few cases of manic-depressive psychosis also were treated with nuclein.

The Solution of Nuclein Employed

The solution for injection, always freshly made, was prepared according to Donath's formula, ¹ viz.: sodium nucleinate, Gm. 10; sodium chloride, Gm. 1; distilled water, Gm. 100. At first a 2-percent solution was used, but later one of 10-percent strength; but still later the author returned to the 2-percent solution, for certain reasons to be explained further along. At the beginning, physiologic salt solution was injected simultaneously with the nuclein, but later this was omitted, since there was no difference in the results obtained.

As a rule, the injections were given every four to eight days. The nuclein administered in one of such courses amounted to 8 to 12 Grams. Later the doses as well as the number of injections were increased, so that

eventually in the course of one such "cure" from 20 to 25 Grams of nuclein would be administered. In a few cases of general paralysis, the course was repeated one or more times, with intervals of a few weeks between, so that in the course of these three or four injection-series the patient received altogether from 35 to 45 Grams of nuclein, and in this way the leukocytic reaction was induced and intermittently maintained over several months.

In general paralysis, the nuclein "cure" was at first combined with more or less energetic antiluetic treatment, according to the nature of the case; but as a rule the following scheme was the one adopted: Before initiating the "cure," some arsenic and iron preparation; next, potassium iodide (1 Gram three times a day) for several months; then simultaneously with the nuclein, or alternately, a mercury preparation and salvarsan, in doses of 0.3 Gram, intramuscularly.

The preparation that seemed to be most suitable here were: arsenferratose, potassium iodide, and enesol (mercury salicylarsenate). In some cases of dementia præcox, it was found convenient to administer, together with the nuclein and arsen-iron, some organitherapeutic preparation, preferably thyreoidin, as a rule.

No local anesthesia was induced before making the injection; still, if the patient was very sensitive or showed dread, a sufficient tolerance was obtained by giving small doses of scopolamine-morphine.

Generally the injections were painful, but especially so the 2-percent solution, owing to the large amount of liquid introduced and the longer duration of the process. Since only fresh sterile solutions were used, not much local irritation developed, while formation of abscesses was completely avoided, excepting in one single case. However, often a painful infiltration, with an erysipelas-like redness of the skin did appear; but this was quickly brought to an end by means of compresses wet with alcohol. [Lundvall declares that the 20 percent nuclein solution, containing also

^{*}This paper, in its rendition into English, has been much condensed from Doctor Hauber's original paper published in the *Zeitschrift fuer die Gesamte Neurologie und Psychiatrie*.

quassine and sodium cinnamate, is not painful.—Ed.]

The Reaction to the Nuclein Injections

The desired reactions—namely, increase temperature and hyperleukocytosis—were promptly obtained in every instance. The average maximum temperature was 38° to 39° C.; but sometimes the temperature went as high as 40° or 41° C., and then was accompanied by chills, nausea, and vomiting. This increase appeared as early as six or eight hours after the injection, and then during the next two or three days it gradually receded to normal.

In patients whose temperature was subnormal, the reaction was interesting, in that the injections were followed by a temporary average increase to normal. In a few cases no temperature rise occurred, even when the doses were rapidly increased; instead, a temporary marked increase of the pulse rate was observed.

Hyperleukocytosis could always be demonstrated, even in those whose temperature failed to rise. The average increase of leukocytes amounted to from 8000 to 20,000. The hyperleukocytosis generally lasted longer than the fever. In the few patients in whom hyperleukocytosis already existed, a corresponding increase of leukocytes in the blood followed the injection.

Precautions Necessary in Treating Paretics

Disagreeable after-effects were seldom observed with the nuclein "cure." A few patients who had received a large number of injections complained for a long while of a drawing and irritating where the injections had been made. This pain was partly due to an abnormal development of the skin about, but which usually disappeared by slow absorption.

In treating psychoses, considerable caution was necessary, owing to the possibility of physical complications. Quiescent tubercles often were seen to flare up. In one patient, the course of the disease was thereby influenced in an unfavorable way. In every instance where the heart was not perfectly sound (myocarditis, coronary sclerosis, aortic aneurism in tabetics and paretics), threatening cardiac signs appeared, such as irregularity, weakness of the pulse, and a marked increase of pulse frequency that did not correspond to the increase of temperature.

By careful selection of the cases and giving prophylactic stimulants, these disagreeable effects later usually were avoided.

In spite of all the care exercised, two of the paretics succumbed quickly after the first nuclein injection. In the first one, profuse diarrhea appeared. In the other patient, the fever caused by the second injection did not, for some inexplicable reason, recede, while, after some time diarrhea also set in. These profuse diarrheas, which could not be checked by any therapeutic means, brought about the end. The impression has been gained, though, that this was not because of any incidental complications, but, rather, that the nuclein injection was harmful and favored the fatal result. Perhaps there was an idiosyncrasy to sodium nucleinate. Kraepelin, as early as 1912, called attention to the existence of such a condition.

One other patient, who had Huntington's chorea, and received the nuclein treatment, also reacted unfavorably to the injections. This patient complained of persistent and violent headache, digestive disturbance, and nausea; his weight rapidly decreased, and at last he refused all food, and an unrestrained state of excitement pulled the patient still further down physically than ever before.

Aside from these unfavorable experiences, the nuclein produced, with a careful choice of the cases and marked individualized treatment, nothing but good results physically.

Paretics Generally Improved

After appropriately regulating the dietary, the general condition of the patients treated was almost always improved; but that this improvement was due to the nuclein treatment was evident in many cases without further proof. The nuclein, in these subjects, proved an excellent tonic: often after the first course of injections the strength of previously decidedly decrepit patients increased rapidly, their appetite improved, digestion more regular, assimilation of food became better, sleep more restful and of longer duration. In this way the loss of weight was checked, and in some cases even a permanent increase in weight was obtained, without any pathologic accumulation of fat masses, particularly in paretics.

This general and prolonged tonic effect consequent upon the nuclein treatment left no doubt in our minds as to this drug's great value, in view of the possibility of its applicability in psychoses for its quieting effect and its ease of utilization; for, by improving the patient's general condition and vitality, the ground would be laid for subsequent periods of intermittent arrest of the disease.

The author is also convinced that the very striking tolerance for the preliminary, and often very severe, mercury treatment—so contrary to previous experiences in paretics—must be ascribed to the influence of the nuclein.

This increased tolerance for mercury after nuclein treatment was strikingly demonstrated particularly in the case of one of our paretics, in which there was a faint suspicion of brain lues. This patient was first treated with mercury without simultaneously receiving nuclein, and although every care was used there followed a rapid physical breakdown, eventuating in a violent paralytic state of excitement. Then he was subjected to a preparatory course with nuclein, in consequence of which he recovered physically; and now this same patient bore a very energetic course of antiluetic treatment remarkably well. At the same time improvement of his psychic condition also occurred.

The tonic effect of the nuclein injections was greatest when a 2-percent solution was used, while a 10-percent solution often failed to give the same result. The author believes that this must be attributed to the larger amount of fluid (that is, physiologic salt solution) introduced when the weaker solution is used.

In the few cases of dementia præcox in which thyreoidin also was administered, no considerable disturbances were observed when directions were followed—that is to say, when the thyroid medication was begun only after stimulation with nuclein.

Nuclein Treatment of Progressive General Paralysis

The author, himself, has treated 36 paretic demented, of whom 9 were in a highly advanced stage. In 3 of the latter, the nuclein injections must be considered to have had a directly harmful effect, while the rest did not react at all. Altogether 27 relatively recent cases of general paralysis were treated, of which 14 (that is, 51.86 percent) were not influenced at all; while the other 13 (that is, 48.15 percent) were very much improved, and all of these could be discharged. However, the tonic action of the nuclein is quite remarkable; for improvement in the patient's general condition never failed to appear, even in very advanced cases and when no specific psychic improvement could be observed.

Many times the marked sedative effect of the nuclein injections appeared very early, and often greatly excited paretics quickly fell into a long-lasting deep sleep after re-

ceiving an injection. Distinct sedative effects also were obtained in the control-experiments with ordinary physiologic salt solution (with or without adrenalin); the symptomatic results from the nuclein injections, though, in every respect were more lasting, since the temporary sedative effect practically always was followed by a prolonged quieting effect. The condition of great excitement and confusion decreased, and the patient became more sociable and more orderly in his behavior. Orientation returned, the sense of place and locality being first; and the disposition became more uniform and more like normal. A certain euphoria remained and it was surprising to see how the memory, which had been lost, was being regained. Never, however, did the symptoms disappear completely, no matter how marked the temporary improvement might be. Complete restoration of mentality never resulted.

The periods of improvement following this treatment were usually very pronounced and occurred more frequently than in the untreated victims. Strictly speaking, it cannot be said, however, that all the periods of temporary improvement observed were results of the nuclein treatment; nevertheless, it may be claimed positively that these spells of improvement were more frequent and more pronounced than they were anterior to the treatment.

Danger of Discharge During Remission

One unsatisfactory feature is that when the patients were discharged during a period of remission (improvement) it was found that not once were the results lasting. Out of the 11 patients mentioned above, 6 came back after an interval of several months, owing to a more or less violent recrudescence of their symptoms. Still, by means of a renewed nuclein course, the acute aggravation of the disease was overcome in all of them, while also a certain quieting effect was obtained. Nevertheless, the progressive deterioration was not arrested.

In the case of totally demented patients, the author hardly expected the nuclein treatment to improve this condition, but he found that it even did more harm than good. In such patients, the best course proved to be to follow the principle of *quieta, non movere*.

Nuclein Treatment in Dementia Præcox

Looking over the literature on the treatment of dementia præcox with nuclein, we see that Lepin has treated 12 cases, of which

3 were slightly improved, and 9 absolutely uninfluenced. Itten had 9 cases, without obtaining any results. Lundvall treated 18 cases with 20-percent sodium-nucleinate solution, to which were added arsenous acid and hetol; 4 of these were cured, 9 were much improved, 2 slightly improved, and 3 uncured. Donath reports 14 cases; 3 were cured, 5 were improved, 3 became worse after temporary remission had taken place, 3 uncured. Donath thinks that the unsuccessful results obtained by Itten were due to the fact that he used, all told, only about 5.8 Grams of nuclein, while his own patients received on an average 14.8 Grams.

The author himself has treated 20 cases of dementia præcox of different types and duration, and of the 20 cases 10 (i. e., 50 percent) remained uninfluenced. However, these were all very advanced, the patients being already considerably demented and prognostically without any prospects.

Two of these 10 patients showed temporary slight improvement; a continuous stupor, which had lasted for months, disappeared quite suddenly after the second nuclein injection, which however did not last. Both patients are now in a very advanced state of dementia.

In 2 of the remaining 10 cases, the treatment has not yet been completed; still, any considerable influence upon their psychic condition has not as yet been observed. Both cases are advanced. As a curiosity, it may be mentioned that one of these patients, after being a catatonic, positively having refused everything for more than a year, now takes food willingly and abundantly. In the third case, the treatment had to be discontinued for special reasons.

The remaining 7 cases (that is, 35 percent) were decidedly improved, all having long intervals of remission. In fact, 4 of these were in such a condition that they were dismissed, as being able to work. In the remaining 3 cases, the improvement was less decided. One of the patients, whose conduct gave very little hope of improvement when he left the institute, recovered later in a surprising way. He was reported perfectly healthy by another physician, and showed any excitement only when under the effects of alcoholic excess.

Nuclein Treatment of Manic-Depressive Insanity

In regard to the treatment of manic-depressive insanity, Lepin is the only investigator who has reported on the nuclein

treatment in psychoses. He treated 13 patients. Of these, 8 were cured, 2 much improved, 7 slightly improved, 2 uninfluenced. Lepin concluded that the old dogma of psychiatry, to the effect that the course of a manic-depressive attack can not be influenced at all, does not hold, after once it had been shown that precisely the melancholic condition was shortened and favorably influenced by his treatment.

The author has used the nuclein treatment in 6 such patients. 3 of them distinctly periodic, 2 melancholic, and 1 with chronic mania. In one case of melancholia, the treatment had only a temporary favorable effect; in the second, no result was obtained. One victim of periodic psychosis was improved and could be dismissed before the end of the full treatment. In the second periodic case, only a temporary effect was obtained. The third received 9.8 Grams of sodium nucleinate, but without showing any favorable result whatever. However, the patient recovered after a long period. The sixth patient was a confirmed maniac. The nuclein did not produce any lasting result, although a certain temporary sedative socializing effect was observed.

Conclusions

1. Sodium nucleinate is entirely harmless when the cases are carefully chosen. It is a very reliable remedy for the artificial induction of the febrile state and of hyperleukocytosis. The desired reaction appears with certainty in a surprising majority of the cases. The individual psychosis groups show no difference in their mode of reaction. The preference for the nuclein treatment lies in the stimulative and marked tonic action of the remedy. The tonic effect to be obtained with nuclein seems to lay the foundation for the subsequent periods of intermission.

In connection with the nuclein treatment, the following adjuvant therapeutic measures are urgently recommended: Individualizing regulation of the diet, open-air regimen, careful dosimetric therapy. Because the effects of the nuclein are solely preparatory, no lasting results or absolute cure can be obtained, even if the treatment be carried out ever so intensively. Perhaps, though, such results might be obtained by the combined treatment with nuclein and other remedies. The combinations thus far tried have not given definite results.

In progressive general paralysis, the very intensive antiluetic treatment made possible by the nuclein stimulation has not fulfilled expectations.

In dementia præcox, the administration of thyreoidin in connection with the nuclein "cure" seems to present better prospects. At all events, further experiments in this direction are very desirable.

2. The increase of the prospects of intermittent improvement in the paralyzes treated by way of preparation with nuclein are striking, as compared with the spontaneous remissions. The improvement obtained with nuclein is, in general, greater, although not different than that occurring spontaneously. Likewise, artificially produced improvement is not a cure of the paresis itself; rather it indicates (as it also does in spontaneous remissions) an overcoming of the acute exacerbation and of the aggravation in the course of the paresis. (Baillarger, Wernicke, Alzheimer, Schroeder.)

A restitution to normal, that is, an absolute cure, does not occur. In most favorable cases, a *status quo ante*, or, the condition which existed before the appearance of the acute attack, is reached. The effect of nuclein is symptomatic. A cure of general paralysis with nuclein is completely excluded.

The advantage of the nuclein treatment is that the average term of life of paretics may be prolonged by the increase of the power of temporary improvements—the length of this latter period, the consequent diminishment of the rapidly progressive tendency of the disease, and the removal of the great danger of acute exacerbations.

3. To answer the question, whether the favorable results obtained in dementia præcox, as above reported, are ascribable exclusively to the nuclein is just as difficult, if not more so, than in the case of progressive general paralysis. Dementia præcox is also inclined, in a higher degree than general paralysis, to spontaneous intermissions. The prognosis is very uncertain, and it can in no case be anticipated with certainty that a remission will occur.

Whether the remissions observed have been artificial or spontaneous, consequently is uncertain. One could not, however, help but get the impression that the nuclein treatment must have been of some advantage in some of the dementia-præcox cases. These, though, refer only to relatively recent cases of the disease; particularly in hebephrenia, in one patient who had reached a good state of remission, the nuclein treatment, combined with a course of thyreoidin treatment, seemed to have a very favorable effect. The treatment was of no advantage in advanced dementia præcox cases, even when prosecuted vigorously.

The possibility is not excluded that through this treatment an increase of the power to improve could be obtained in dementia præcox, as it has been in paresis. If this be the case, and if it can be proven by further experiments, then we have in nuclein an important remedy that should not be underestimated, because—as experience has shown—periods of temporary mental improvement in dementia præcox often lead to a cessation of the disease and a cure of the disease.

4. The author has had too few cases of manic-depressive insanity to arrive at any definite conclusion. The treatment of these few cases with nuclein did not give satisfactory results. He has ceased to use it for this purpose.

[The preceding article, we believe, will be of peculiar interest to every person interested in the treatment of insanity, especially since the appearance of Dr. Bayard Holmes's paper in the May number of CLINICAL MEDICINE, in which Lundvall's method of treating dementia præcox with nuclein was so clearly and entertainingly presented. Hauber's article, the English version of which herewith is presented, assuredly is an important contribution to nuclein therapy, and, if taken in conjunction with the contributions of Lundvall and other European psychiatrists, it clearly shows that in nuclein we have a remedy of exceeding importance.

While of course it is too much to expect that this new mode of attack should prove curative in paresis—a disease which is usually considered beyond hope of successful treatment—the fact that at least a certain improvement follows the employment of this remedy lends credence to the hope that some time it may be possible to master it, providing individuals so afflicted can be seen sufficiently early.

In the case of dementia præcox, the evidence is accumulating that brilliant results are obtainable with nuclein. Dr. Bayard Holmes, who has used it more than anyone else in this country, is an enthusiast concerning its possibilities; while we ourselves are convinced that when once physicians know how to handle the drug, and know how to handle their cases, a very considerable percentage of these unfortunate young people may actually be cured.

Personally, we are of the opinion that a built-up solution of nuclein, similar in composition to that employed by Lundvall, will assure better results both in dementia præcox

and in paresis of the insane than will an extemporized normal-salt solution like that employed by Donath. The Lundvall solution contains other substances stimulating leukocytosis besides the nuclein; the quassin, for instance—as Doctor Lundvall has informed us in a personal letter—being added for that purpose. So, also, the sodium cinnamate stimulates leukocytosis, although Lundvall has recently informed us that he is now discontinuing this substance and substituting for it arsenous acid; which latter is powerfully tonic and thus adds to the reconstructive power of the other ingredients of the formula.

We venture to hope that among those who

may read this article by Hauber there may be some who will feel inclined to try out this method of treatment thoroughly: making a scientific study of the blood-picture in all cases, verifying the diagnosis by the Abderhalden and other appropriate tests, and keeping a close watch upon the diet, exercise, exposure to sun, condition of the alimentary canal, and the various other factors necessarily playing an important part in contributing to improvement and eventual recovery. It is with the expectation that the publication of these articles may stimulate investigations along this line in America that we have submitted them to the readers of our journal.—ED.

Nuclein in Paralysis Agitans

Parkinson's disease (paralysis agitans) is so resistant to treatment that any method of handling cases of this kind that promises benefit deserves study. Buia has recently quoted a series of cases of this disease in which nuclein was used. (See *Compt. Rend. d. l. Soc. d. Biol.*, 1914, p. 507.)

Buia employs a 10-percent solution of sodium nucleinate in physiologic serum. He gave it by mouth, hypodermically, and also intravenously. When taken internally, no effects were observed. Administered subcutaneously, the maximum dose was 40 centigrams (6 grains); beginning, however, with a much smaller dose and then increasing by 5 centigrams every two days, until this maximum was reached. Five patients were treated in this way, and all of them were benefited.

However, the best results were obtained when the remedy was given by the intravenous route, the same solution being employed. Sometimes the immediate response was slight; in others, there was a well-marked rise of temperature, with slight chill, while in a

third there was observed some diminution of tremor, a lessening of the muscular rigidity and in the rise of temperature, the latter subsiding to normal in about four hours, with some rise in the blood pressure.

In the second class of patients, there was general improvement following the immediate symptoms produced by the injection of the nuclein. Continuance of this treatment was marked by definite psychic improvement, accompanied by lessening of tremor and increase in muscular force. This benefit exhibited some degree of permanency. No untoward symptoms developed, although in some instances nausea, vomiting, and vertigo developed when more than 35 or 40 centigrams of the remedy was administered. There was occasional tachycardia, dyspnea, and headache. However, these depressing symptoms are not observed when the drug is given in moderate doses.

We should like to see the Lundvall solution, containing nuclein, arsenic and quassine, tried thoroughly in some of these cases. It should prove of value.

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